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The Lederle Bulletin

January 1924

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511 FIFTH AVENUE, NEW YORK

The Lederle Bulletin

JANUARY 1924

Transformation of the Intestinal Flora

IN spite of the published reports of various investigators showing that Bacillus bulgaricus will not live, grow and multiply in the intestinal tract, the use of this organism for the purpose of replacing the harmful intestinal bacteria has continued to increase. Recently, however, the very thorough investigations of Rettger and Cheplin into the possibilities of establishing the Bacillus bulgaricus in the intestinal tract of both white rats and man have definitely proven that it cannot be done. Their exhaustive researches in intestinal bacteriology which were conducted in the Sheffield Bacteriological Laboratory of Yale University proved that in not one instance could a single Bacillus bulgaricus be isolated from the feces. Therefore, it would seem that their work has finally settled the question and proven conclusively that the Bacillus bulgaricus cannot be propagated in the intestine of either man or animal.

One should bear in mind, however, that the failure of Bacillus bulgaricus to live and grow in the intestine and thus displace the harmful bacteria does not in any sense refute the theory of intestinal toxemia, nor the theory that such toxemia can be controlled by substituting harmless for the harmful bacteria in the intestine.

In the new-born infant, the intestinal tract is free from germs; but within five to ten hours after birth, bacteria can be demonstrated. If the infant is breast-fed exclusively, the intestinal flora is simple and uniform and invariably consists of acid-producing bacteria called "aciduric bacteria." Of these, the bacillus

bifidus predominates with the Bacillus Acidophilus present in smaller proportions. On the other hand, as soon as the infant is fed on other foods or if it is bottle-fed, Bacillus Acidophilus becomes the dominant organism and the bacillus bifidus is much less numerous. Usually, by the time breast feeding is discontinued and a diet composed chiefly of cow's milk is substituted, the flora consists almost entirely of Bacillus Acidophilus with only a small proportion of the bacillus bifidus. Such a flora, of course, exists only under normal or healthy conditions in the intestinal canal.

During the next two or three years, or as long as milk forms a large part of the diet, Bacillus Acidophilus remains the predominant organism; but as the child grows older and the diet becomes more varied with a reduction in the quantity of milk in the diet, the intestinal flora becomes more and more complex and the simple aciduric bacteria give way to a variety of other types. According to Bass,[1] the Bacillus Acidophilus usually constitutes from none up to five or six per cent of the living bacteria present in the intestinal tract of normal adults. The other bacterial types, such as the bacillus coli, cause putrefaction of the food with the production of gas and toxic substances, resulting in constipation and intestinal toxemia. Under conditions of a mixed diet, the predominance of the bacillus coli among the intestinal bacteria continues from later childhood to adult life.

The ratio of the number of bacillus coli to the Bacillus Acidophilus has been used by Cannon[2] to indicate the extent of putrefaction in the intestine. The larger the number of Bacillus Acidophilus which can be maintained, the less other bacteria will be present and, therefore, the less putrefaction and intoxication will occur. Clinical and bacteriological studies have shown that the Bacillus Acidophilus, which is a normal inhabitant of the intestinal tract and the predominant organism at a certain period of early life in most normal individuals, will thrive better than any other lactic acid organism when introduced into the lower intestine by way of the mouth.

When living milk cultures of the Bacillus Acidophilus are given in large quantities, this organism soon becomes the predominant type of bacteria in the intestines; approximating if not equaling the condition which exists in infancy and early

[1] Bass, "Transformation of the Intestinal Flora"; *Annals Clin. Med.*, July, 1922.

[2] Cannon, "The Effects of Diet on Intestinal Flora"; *Jour. Infect. Dis.*, Oct., 1921.

childhood. As long as the Bacillus Acidophilus is maintained as the predominant organism in the intestinal flora, a healthy functioning of the intestine is favored and the general bodily health promoted.

Microscopically, Bacillus Acidophilus is almost indistinguishable from Bacillus bulgaricus; but culturally these organisms do not act upon the same sugars. Moreover, Bacillus Acidophilus produces relatively little acid in milk (less than 1 per cent), whereas Bacillus bulgaricus may produce as much as 3 per cent.

The investigations of Rettger and Cheplin[3] have shown that:

> "Milk cultures of Bacillus Acidophilus have proven themselves to be particularly effective in transforming the intestinal flora of man. In some instances 500 cubic centimeters were sufficient to bring about simplification with the desired elimination of the non-aciduric forms. A total of 1,000 cubic centimeters taken daily in two applications in every instance brought about the transformation in the course of a very few days."

Recently, a note of warning has been sounded by Bass[4] who states:

> "Commercial interests have already placed upon the market B. Acidophilus in the form of tablets, capsules and liquids, and physicians are prescribing them. I recently examined some of these preparations on the market to determine the number of viable B. Acidophilus contained therein.
>
> "In the instance of tablets, none of those examined was found to contain as many as 1,000 viable bacteria of any kind per tablet. If it should be granted that all the viable bacteria present were B. Acidophilus, it would take more than 1,000,000,000 tablets, or more than 20 tons, to contain as many bacilli as are contained in 1,000 cc, or the usual daily dose, of the acidophilus milk; the quantity found, by most investigators at least, to be necessary to transform the flora. Bacteria were more numerous in the commercial liquid cultures examined. If they were all B. Acidophilus, a patient would have to drink only about seven or eight gallons daily to get as many as he would in 1,000 cc of the acidophilus milk culture."

Bacillus Acidophilus Milk is recommended in the treatment of intestinal disturbances due to putrefactive changes; in chronic colitis, chronic constipation, rheumatic conditions, sprue, eczema and acne; and in typhoid fever, dysentery and cholera. Also in toxic diarrheas of infants and in infant feeding.

[3] RETTGER AND CHEPLIN, "A Treatise on the Transformation of the Intestinal Flora"; *Yale University Press*, 1921.

[4] BASS, "Transformation of the Intestinal Flora"; *Southern Medical Journal*, Jan., 1923.

Serum Treatment of Lobar Pneumonia

In a recent paper by Camac, a clinical report is given of 603 cases of all types of lobar pneumonia treated in the military service and in Gouveneur Hospital, New York City. Of this total number, 244 were treated with polyvalent antipneumococcic serum resulting in a mortality of 13.9 per cent; while 359 cases treated without serum showed a mortality of 29.8 per cent.

Camac states that treatment with polyvalent antipneumococcic serum was adopted at Gouveneur Hospital because of the low mortality and freedom from clinical toxic manifestations which resulted from its use in the military service. In his paper, several interesting facts are brought out:

(1) Sputum differentiation for types could not be carried out in all cases, due to lack of facilities. But even in those cases where the sputum was differentiated, serum was given first because "we have regarded the prompt administration of antipneumococcic serum in the same way as one regards the prompt administration of antimeningococcic serum in cases showing meningeal involvement."

(2) In the absence of routine sputum differentiation, the report includes all cases of lobar consolidation of whatever bacteriology. The value of serum treatment for Type I pneumonia has been frequently demonstrated, but the practicability of using serum for cases of Type II and Type III pneumonia has been open to question. Therefore, Camac's results assume greater significance. He states: "That polyvalent serum is efficacious in the other types we are convinced from clinical observation, though we recognize that this has not been proved by laboratory investigation." However, he goes on to say: "The research laboratory worker is compelled to limit his statements to what is demonstrable by laboratory tests. The clinician, at the bedside, *lacking these laboratory proofs*, makes observations with regard to duration of the disease, well-being of the patient, that is, degree of toxic manifestations, limitation of the pathological processes, recovery, mortality, etc., all of which, if studied in a sufficiently large number of cases and within strict limitations, constitute *clinical evidence* which may precede and lead to subsequent laboratory proof."

(3) In analyzing these cases, the author points out that "the prognosis becomes increasingly less favorable when serum is begun *after the third day of the disease*. Serum administered in the first twenty-four

to thirty-six hours offers the best prognosis."

For the past seven years, Camac has been Medical Director of Gouverneur Hospital and is Professor of Medicine in the New York Polyclinic Medical School and Hospital. The fact that the manuscript of his paper was reviewed by Dr. Rufus Cole before publication lends additional weight and importance to Camac's observations.

New Method of Administering Diphtheria Antitoxin

Dr. E. S. Platou, who is connected with the Willard Parker Hospital and the Research Laboratory of the New York City Department of Health, has just published the results of a comparative study of the usual methods of administering antitoxin as contrasted with the intraperitoneal method.

For years there has been considerable discussion as to the most suitable means of administering antitoxin. The absorptive power of the peritoneum, previously shown by many observers, suggested to Platou this area as a possible route for antitoxin. The most favorable site for the introduction of the needle is through the linea alba just below the umbilicus. The safety of the procedure had been proved; so it only remained to be demonstrated that the serum itself was non-irritating.

After preliminary tests on rabbits showed that much more antitoxin was absorbed by the blood during the first six hours when given intraperitoneally than when injected intramuscularly, Platou proceeded to make a clinical application on 21 cases of diphtheria at the Willard Parker Hospital. As a result of this clinical study, he concludes that (1) local discomfort, an annoying factor in the subcutaneous and intramuscular methods, is absent in the intraperitoneal method; (2) early absorption of antitoxin after intraperitoneal injection is approximately five times greater than after intramuscular injection, within an hour it is more than sufficient to neutralize the circulating toxin in the blood of any case of diphtheria; and (3) intraperitoneal administration of antitoxin is a safe and simple procedure.

Platou recommends the intraperitoneal method particularly (*a*) in advanced cases where suitable veins for intravenous administration are lacking; and (*b*) in moderately advanced cases in which intravenous injection is not considered necessary or advisable but where more rapid absorption is desired than can be obtained by the intramuscular method.

Hay-Fever Prevented with Pollen Antigens

As early as 1911, medical research workers had successfully treated hay-fever patients with extracts of pollen. This early work was done with freshly prepared extracts and no provision was made for the preservation of these extracts in stable form. Hence, the general application of this treatment by the practicing physician was not at that time practicable.

In 1914, researches conducted in the Lederle Antitoxin Laboratories resulted in the perfection of pollen antigens in stable and standardized solution. The physician for the first time was thus afforded a means for the scientific treatment of his hay-ever patients. The pollen antigens are prepared in a stable solution by extracting the mature pollen grains in 66⅔ per cent glycerol and 33⅓ per cent saturated sodium chloride solution. Such glycerolated pollen antigens have proved remarkably stable and more potent than those obtained by any other method of extraction.

It has been clinically demonstrated that hay-fever can, in many cases, be prevented or alleviated by treatment with the glycerolated pollen antigen prepared from the particular pollen to which the person is sensitive. In 1922, Clock reported an analysis of 1,578 clinical reports from physicians in all sections of the United States who had used the glycerolated pollen antigen during five consecutive years. This analysis shows an average protection or relief from hay-fever symptoms in 84 per cent of cases with a remarkable uniformity of favorable results each year in every locality.

Recently, the results of the investigations of the United States Public Health Service into the status of preventive treatment of seasonable hay-fever were published in the *Journal of the American Medical Association*. This investigation included an analysis of the various methods of preparing and testing pollen extracts. It will be of interest to physicians that this investigation confirms the work originally carried out in the Lederle Antitoxin Laboratories; also that the method for the preparation and testing of pollen antigens developed in the Lederle Antitoxin Laboratories and reported by Dr. Clock was found satisfactory, as shown by the following excerpt from the published report of the Public Health Service expert:

> "Clock is deserving of much credit for calling attention to the fact that chemical analysis fails to demonstrate the antigenic qualities of pollen extracts. Such analysis reveals only the amount of pollen

protein present in solution. Clock has shown that a practical method of determining the antigenic properties of pollen extract is by means of the complement fixation test. . . . He has, furthermore, devised a method of preparing a stable antigen by the use of concentrated salt solution and glycerol. Pollen extracts, prepared by his method, have remained for fourteen months without loss of complement binding capacity. With his glycerolated pollen antigen Clock obtained relief from symptoms in 84% of 1578 cases."

Refrigeration of Biological Products

For purposes of commercial convenience, the argument has often been advanced that it is not necessary to keep biological products under refrigeration. Standard tests applied to many biological products will accurately determine their potency; but tests applied to many others are less certain to accurately measure their potency.

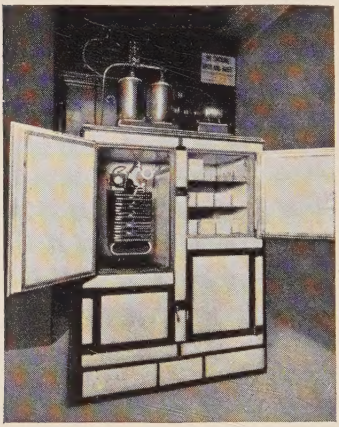
In the study of the effect of different conditions of storage upon the potency of biological products, it has been found that all those products whose potency can be most accurately determined, definitely show a greater loss of potency when stored at warm temperatures than when stored under proper refrigeration.

The deterioration of antitoxins outside of cold storage is well known. Thus, if kept at room temperature (20° to 30° C), it is generally conceded that antitoxin will lose approximately 25 per cent of its potency per year. However, under conditions of good refrigeration (5° to 10° C), the loss of potency will be less than 10 per cent per year. This fact is recognized by the United States Public Health Service which requires that all antitoxins be filled with 20 per cent excess to insure the full potency at the end of one year.

Refrigerator with drawers on sides for storing biological products, chilled with ice in upper middle compartment

Elgin has shown that hot and especially variable temperatures

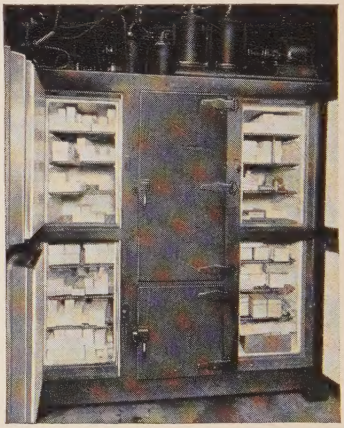
speedily injure vaccine virus. Furthermore, it has been shown that glycerolated vaccine virus properly prepared and stored at a temperature below 10° C deteriorates slowly; but as the surrounding temperature rises above this point, rapid degeneration of the vaccine becomes



Refrigerator with mechanical refrigerating plant; cooling unit in upper left compartment. Shelves at right for storing biological products

pronounced. Vaccine virus stored below freezing temperature will apparently remain active for a considerable time without any deterioration. This point is well emphasized in the following instructions issued by the Florida State Board of Health:

"Vaccine should be kept on ice until used. Vaccine not kept at a low temperature soon becomes inert and will not "take." Vaccine kept at 98° F (37° C) three to four days was dead. (This is body temperature and about the temperature at which the vaccine would be kept if carried in the pocket.) Vaccine kept at 70° F (21° C) one to three weeks was weakened but not dead. Vaccine kept at 50° F (10° C) three to seven months was still active. (This is about refrigerator temperature.) Vaccine kept at 10° F (−12° C) four years was still active."



Refrigerator with mechanical refrigerating plant; cooling unit in upper middle compartment. Shelves on both sides for storing biological products

The expiration date stamped on the package is a reliable guide for judging the activity of the vaccine only when it is continuously kept

on ice. During the summer months, special attention must be given to the storage and shipping of vaccine virus; for if its vitality has at any time been weakened by improper storage or handling, subsequent storage on ice will not restore the usefullness of the product.

Experiments conducted at the Hygienic Laboratory by McCoy and Bengtson demonstrated that typhoid vaccine stored at refrigerator temperature (5° C) showed no trace of deterioration for nine months. At the end of eighteen months, vaccine stored at refrigerator temperature (5° C) showed less deterioration than vaccine which had been stored for six months at room temperature (20° to 30° C).

In view of the above facts, the practitioner should see to it that all biological products which he desires to use have been kept under proper refrigeration. Otherwise, he cannot hope to secure satisfactory clinical results from biological therapy.

The Lederle Bulletin

A concise presentation of authoritative information concerning the practical application and clinical value of biological therapy.

Published by

LEDERLE ANTITOXIN LABORATORIES

511 FIFTH AVE NEW YORK CITY

Universal Diphtheria Immunization Now Practical

With the original formula of toxin-antitoxin, containing three L plus doses of toxin, Park demonstrated conclusively the value of diphtheria immunization. In over 90 per cent of the children immunized in the public schools of New York City (some 500,000 children), the immunity lasted over six years and possibly will continue throughout life. It was found, however, that the original formula was impractical for universal immunization because of the severe reactions produced in adults.

Park and his co-workers at the Research Laboratory of the New York City Department of Health have modified the formula to contain only one-tenth L plus dose of toxin. Park's studies show that this new formula produces an immunity equal to that established by the former product, and that *no severe reactions occur* even in older children and adults. Hence, this improved product will permit of universal immunization against diphtheria.

Immunization with toxin-antitoxin consists of three doses injected deeply into the subcutaneous tissue of the upper arm, over the insertion

of the deltoid muscle. The doses are given at intervals of one week, each dose consisting of 1 cc, both for children and adults.

Diphtheria immunization is especially useful for (*a*) all children from six months to six years of age, for during this age period the sus-

DIPHTHERIA IMMUNIZATION

1. Children of Public School No. 50, Brooklyn, N. Y., in line waiting to be immunized.

2. Nurse sterilizing skin of forearm in preparation for the Shick test.

3. Dr. M. C. Schroeder, assistant director of the Research Laboratory of the New York City Department of Health, applying the Schick test on child's forearm.

4. Dr. M. C. Schroeder, assistant director of the Research Laboratory of the New York City Department of Health, reading a positive Schick test.

5. (Right) Attendant sterilizing skin with iodin previous to immunization with toxin-antitoxin. (Left) Nurse immunizing child with toxin-antitoxin.

ceptibility to diphtheria as well as the mortality is greatest. By systematic immunization of children between these ages, diphtheria could be wiped out in a few years. (*b*) School children from six to nineteen years of age usually come in contact with diphtheria each year and carry

the infection home. No logical or practical method of eradicating diphtheria can be carried out without including the routine immunization of school children. (*c*) Those adults who come in contact with diphtheria and are constantly exposed to the infection, including physicians, nurses and hospital attendants. (*d*) Persons who, due to exposure or infection, have received treatment with diphtheria antitoxin as a curative or prophylactic measure. Four weeks after the antitoxin is given, immunization of such persons should be carried out with toxin-antitoxin.

The Schick Test

In the earlier studies of the use of toxin-antitoxin for immunization against diphtheria, the Schick test was first applied to eliminate those persons who possess sufficient immunity to protect them against the disease. The first practical application of the Schick test on a large scale in this country was carried out by Park and his co-workers at the Research Laboratory of the New York City Department of Health. As a result of this work, it was found that between the ages of six months and six years, as high as 70 per cent of children may be susceptible to diphtheria; but from six to nineteen years of age, the susceptibility gradually decreases until in adult life it is found in only 15 per cent of those living in cities and in about 30 per cent of those living in the country.

The combined use of the Schick test and toxin-antitoxin for school work entailed a considerable amount of work. The percentage of positive reactors to the Schick test in children under six years of age is so high (over 65 per cent) that in order to place the diphtheria preventive work of a city on a more practical basis, the New York City Department of Health advises that the procedure for the school physician may be simplified by omitting the preliminary Schick test in children of preschool age and also by immunizing all children in the incoming classes with toxin-antitoxin.

The Schick test is now advocated by the New York City Department of Health chiefly for the purpose of proving the development of immunity after immunization with toxin-antitoxin. For this purpose, the test is applied about six months after completion of the immunization. By this means, it will be found that a small percentage of immunized persons may have failed to develop the required immunity, and these should be re-immunized with toxin-antitoxin in order to render them immune.

Another practical application of

the Schick test is to determine susceptibility to diphtheria among older children and adults who are liable to be exposed to the infection; such as patients, nurses and resident staff in general and contagious disease hospitals. If such persons show a positive reaction to the Schick test, they may be rendered immune to diphtheria by immunizing them with toxin-antitoxin. The improved formula of toxin-antitoxin which was introduced last year permits the immunization of older children and adults without danger of the severe reactions which occasionally followed the use of the toxin-antitoxin mixture made according to the original formula.

Treatment of Acne

At the annual session of the American Medical Association in San Francisco, Dr. Howard Fox, Professor of Dermatology at the New York Polyclinic Medical School and Hospital presented a very comprehensive paper in which the therapeutic value of the roentgen ray was compared with vaccines. He points out that the pathology of acne consists essentially in a functional over-activity of the sebaceous glands, combined with a follicular hyperkeratosis. Owing to its inhibitory action on the reproduction of certain types of cells, the roentgen ray is an agent that will inhibit the over-activity of the cells of the sebaceous and follicular openings. This statement is substantiated by the results obtained by Fox in 191 cases of acne treated with the roentgen ray. As a result of his experience, Fox has come to the conclusion that, except in mild cases, nothing but time and the roentgen ray will effect a permanent cure of acne.

In an attempt to learn the opinions of some representative dermatologists in regard to the vaccine treatment of acne, Fox sent a questionnaire to members of the American Dermatological Association. Replies were received from 71 out of the 79 members. Of these, 62 stated that they had used acne bacillus vaccines, of whom two considered them of great value "in certain cases," 30 of some value and 30 of no value. The mixed vaccines (of acne bacillus and staphylococcus albus, aureus, etc.) had been used by 63 of the correspondents, of whom 5 had found them of great value "in certain instances and in chronic indurated types," 42 of some value and 16 of no value.

Fox says that whatever value these vaccines may have is restricted to their use in selected cases, chiefly of the pustular type. In the treatment of acne vulgaris he believes that the roentgen ray is far superior to vaccines.

The Intravenous Administration of Serum

The serum should be carefully warmed to body temperature by placing the glass container in warm water as near 100° F as possible (a higher temperature will coagulate the serum).

Place a tourniquet (a bandage or piece of strong rubber tubing may be used for this purpose) around the upper arm. This impedes the flow of venous blood and causes the superficial veins at the bend of the elbow to distend and become prominent. The median vein of the forearm divides at the bend of the elbow into a fork or Y; the inner branch being the median basilic vein and the outer branch the median cephalic vein. Either of these branches may be used for administering the serum.

INTRAVENOUS TECHNIC

Tourniquet (bandage) around upper arm. Intravenous needle inserted into median basilic vein and blood escaping from hub of needle.

Sterilize the skin over the vein by applying iodine. With the intravenous needle held almost parallel to the surface of the skin and pointed in the direction of the upper arm, force the point of the needle through the skin and upper wall of the vein. If the point of the needle is in the lumen of the vein, blood will appear at the hub of the needle. Now remove the tourniquet from the upper arm before proceeding to introduce serum into the vein. Adjust the rubber tubing to the glass cylinder and allow serum to escape from the free end of tubing, thus expelling all air from the tube. Then firmly insert the metal slip joint end of rubber tubing into hub of needle. Administration of the serum should proceed slowly, by gravity, at the rate of 1 cc per minute for the first 15 minutes after which the rate may be increased.

For the intravenous administra-

tion of comparatively small amounts of serum which are supplied in sterile syringes (such as diphtheria antitoxin) proceed as follows: Warm the serum to body temperature; apply a tourniquet, and sterilize the skin as before. Attach the needle to the syringe and push the piston forward until the air is expelled from the syringe barrel. With the needle attached to the syringe, insert the needle into the vein in the manner previously described. Gently pull back the piston of the syringe; and if the point of needle is in the lumen of the vein, blood will be withdrawn into the syringe barrel. Now remove the tourniquet and proceed to inject the serum slowly.

INTRAVENOUS TECHNIC

Tourniquet removed from arm. Intravenous outfit attached to needle (previously inserted into vein) and serum being introduced into vein by gravity

Desensitization

In all cases in which serum therapy is to be given, make careful inquiry as to a history of asthma, hay-fever, urticaria or previous administration of horse serum.

Patients who present such a history should be tested for sensitization by injecting intracutaneously in the forearm 0.05 cc of serum previously diluted 1:10 with salt solution. If the patient is sensitive, usually within five minutes an urticarial wheal begins to develop which may increase in size up to that of a half dollar; the wheal in turn being surrounded by a larger area of erythema. The reaction usually reaches its maximum within an hour and fades rapidly.

If such a reaction occurs, the patient should be desensitized by injecting 0.5 cc of serum subcutaneously in the interscapular region. Half an hour later, a similar dose may be given intravenously before giving the regular or therapeutic dose of serum. The full therapeutic dose of serum should be injected into

the vein very slowly, beginning with ¼ cc during the first minute; and the first 15 cc should be cautiously injected at a rate not exceeding 1 cc per minute. The remainder may be allowed to flow in more rapidly.

Such procedures, however, mean loss of time. Where the serum is urgently indicated, as in laryngeal diphtheria, tetanus or lobar pneumonia, the danger from the disease faroutweighs any danger from serum shock and thefulltherapeutic dose of serum should be given at once. Under such conditions, the possibility of harmful effects from serum administration may be reduced to a minimum by allowing a few drops of serum to enter the vein very slowly and then interrupt the administration for several minutes. Then allow an additional few drops of serum to flow into the vein; at least 15 minutes being consumed in administering the first few cubic centimeters. If no reaction occurs, the rest of the serum may be given without fear. Severe reactions may be controlled by epinephrin (1:1,000 solution) and atropin injected hypodermically.

INTRAVENOUS TECHNIC

Needle, attached to syringe, inserted into median basilic vein and serum being introduced slowly into vein from piston syringe

Smallpox and Vaccination

In a recent letter to the *New York Times*, Mr. Louis I. Dublin, statistician of the Metropolitan Life Insurance Company, estimated that there are at least 100,000 cases of smallpox in the United States each year. He points out that the disease hasbeen of the virulent type recently in the MiddleWest, and forecasts that an outbreak is about due in the Northern and Eastern States where few cases of the disease have appeared in recent years. Moreover, Mr. Dublin stresses the point that the virulence of the disease is continuously on the increase; and he cites the fact that in a group of 246 cities of the United States, the case-fatality rate in 1922 was close to six per cent, while in

1921 it was a little over one per cent.

The United States Public Health Service recommends the multiple puncture method of vaccination as one of three methods calculated to secure best results. The puncture method is the surest safeguard against infection, for there is no open wound. It leaves practically no scar; hence has an added advantage when vaccinating girls, and it is the safest procedure in vaccinating infants and small children.

A drop of virus is placed on the cleansed skin of the upper arm. A sterile needle is held nearly parallel with the skin and the point of the needle is pressed through the drop of virus so as to make about six oblique pricks or shallow punctures through the epidermis. The punctures should be confined to an area not more than ⅛ inch in diameter. The surplus virus on the surface of the skin may then be wiped off. No shield or other dressing should be applied.

Expelling vaccine virus from capillary tube onto cleansed skin

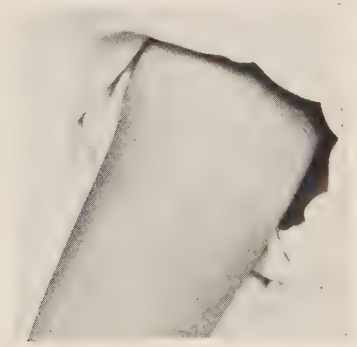
Making multiple punctures with needle point pressed through drop of virus

The Dreyer Tuberculosis Vaccine

The medical world has been keenly interested in the report of the researches conducted by Professor Dreyer of the Department of Pathology in Oxford University,

England. He has produced a so-called "defatted" tuberculosis vaccine.

It has long been known that the tubercle bacillus has a coating of waxy or fatty material, generally called lipoidal substance. Experiments conducted in this country and elsewhere seem to indicate that the virulence of bacteria depends to some extent upon the concentration of such lipoids in their coats or capsules. Dreyer has pointed out that these substances protect the bacterial proteins and prevent their liberation from the body of the bacterium, thus checking or completely stopping the production of the immunity reaction in the infected individual.



Scar resulting from the usual scratch method of vaccination

Arrow points to scar, almost invisible, resulting from multiple puncture method of vaccination

The method devised by Dreyer embraces the use of formaldehyde and acetone to remove the lipoidal elements from the bacteria. This method was chosen because the bacteria are commonly prepared for staining by such treatment; and Dreyer reasoned that since these two chemicals would remove the fatty material and allow the bacterial protein to take the stain, such a method would probably make it possible to obtain the pure bacterial protein for purposes of making a vaccine.

While the work is still in the experimental stage, yet such experimental evidence as is available indicates that the injection of such a defatted vaccine produces immune substances. Animal experiments supplemented by the treatment of

sixty human patients in the London Hospital tend to show, in the opinion of those conducting the experiments, that "improvement has taken place in nearly all cases and is of the order which exceeds obviously that obtainable by any other form of treatment."

As stated in an editorial of the *Journal of the American Medical Association*, the experiments of Dreyer are scientific and have good theoretical basis. Future developments will be watched with great interest.

Unusual Applications of Pituitary Extract

Pituitary extract has been extensively used for many years to stimulate the uterine contractions in cases of inertia. Likewise, its use for surgical shock and intestinal stasis is constantly increasing. Since pituitary extract has been used with success in these conditions, any additional application of the product ought to be of interest to the practitioner; but especially the fact that it will produce therapeutic effects when absorbed from the respiratory or gastrointestinal mucous membrane.

(1) Incontinence of Urine

Pepper reports 19 cases of nocturnal incontinence of urine successfully treated with pituitary extract. Ten of these cases were children, a few young men with both day and night incontinence and five or six men of 38 to 42 years of age with exclusively nocturnal incontinence. In all of these patients, prompt relief of the incontinence followed injections of pituitary extract. There was no recurrence of the incontinence three or four months later.

According to Pepper, it seems improbable that these results are brought about by a lessening of diuresis because of the transitory nature of this reaction to pituitary extract. He believes that the good results obtained with pituitary extract in this condition may be due to the elective contracting influence of pituitary extract on the non-striated muscle fibres of the sphincter of the urinary bladder. He believes the treatment deserves a trial.

(2) Diabetes Insipidus

Allan and Sherrill used pituitary extract in connection with the dietetic treatment of diabetes insipidus. They found that pituitary extract, when administered subcutaneously or by nasal spray, reduced the thirst and polyuria and raised the concentration of the urine. Water retention thus occurred when the intake of water was

constant. Since pituitary extract is known to reduce the urine similarly in normal persons and animals, Allan and Sherrill are inclined to believe that these results in diabetes insipidus represent a pharmacological action rather than a true hormonal substitution.

(3) Oral Administration

Animal experiments conducted by Hamill have proved that pituitary extract administered by mouth will cause the characteristic uterine contractions. Absorption of the extract takes place from the stomach and is more rapid when the stomach is full and rapidly digesting. Large doses produce colicky contractions of the intestine and vomiting.

Clinical evidence is in agreement with these animal experiments, for oral administration of the extract to the human subject produces similar effects.

Prophylactic Value of Pneumonia Vaccines

The great prevalence of respiratory diseases during the winter of 1922–23, caused the Public Health Committee of the New York Academy of Medicine to inquire into the prophylactic value of pneumonia vaccines.

In addition to a study of the literature, the Committee held a conference with a number of experts in this field, including Drs. William H. Park, Director of the Research Laboratories of the New York City Department of Health; Augustus B. Wadsworth, Director of the Bureau of Laboratories of the New York State Department of Health; Alphonse R. Dochez of the Department of Practice of Medicine in Columbia University and Russell L. Cecil of Rockefeller Institute.

In their report, the Committee states:

> "Vaccines have some value against three of the fixed bacteriological types of lobar pneumonia. The duration of the immunity secured is probably not over six months. Vaccination does no harm and there have been no fatal or serious results reported. In order to be complete the inoculation must be given in three doses. There is a definite indication for the use of these vaccines in persons particularly exposed to pneumonia or coming in continuous contact with it. Inasmuch as the prevention of pneumonia by inoculation is still in the experimental stage and inasmuch as there are many preparations put on the market which are of doubtful value, the promiscuous use of vaccines should not be encouraged."

Make Vaccination Popular

THE United States Public Health Service recommends the multiple puncture method of vaccination as one of three methods calculated to secure best results. The puncture method is the surest safeguard against infection, for there is no open wound. It leaves practically no scar; hence has an added advantage when vaccinating girls, and is the safest procedure in vaccinating infants and small children.

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is supplied in glass capillary tubes with rubber bulb and a sterile needle for each vaccination, which permits vaccination by the puncture method.

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Park and his co-workers at the Research Laboratory of the New York City Department of Health have modified the formula to contain only one-tenth L plus dose of toxin.

Their studies show that this new formula confers an immunity equal to that established by the former product, and that no severe reactions occur even in older children or adults. Hence, this improved product will permit of universal immunization against diphtheria.

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